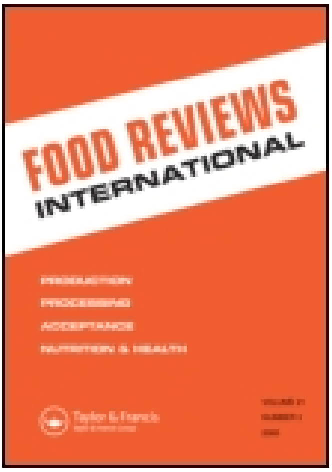

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Sorghum: An Underutilized Cereal Whole Grain with the Potential to Assist in the Prevention of Chronic Disease

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Sorghum is an important cereal grain food, grown globally, that is rich in nutrients, dietary fiber, and bioactive components yet is considered of low value to humans and often used as an animal feed. This review provides an overview of key sorghum grain components, including starches, dietary fiber, protein, lipids, and phytochemicals, with functional properties that have potential to impact on health. Though acknowledging the impact of the whole food will reflect the synergy between the components, studies of these components implicate effects on energy balance, glycemic control, lipids, gut microbiota, and cell-mediated immune responses, including antioxidant and anti-inflammatory effects. For these to be confirmed as contributory effects from sorghum consumption, evidence from quality randomized controlled trials is required. If proven effective, there may be a role for sorghum grain–based diets to assist in the prevention of chronic diseases such as diabetes, obesity, and heart disease. Future research addressing effects of sorghum consumption may help drive a paradigm shift from sorghum as a low value food to a potentially health-promoting, highly valued human grain food.

Keywords Cereal, Health, Nutrition, Sorghum, Whole grain

Introduction

Cereal whole grains are significant contributors to energy, nutrients, and dietary fiber in the human diet and are important for health. Numerous prospective studies demonstrate that regular consumption of whole grains lowers the risk of heart disease and diabetes by 20–30%,(1,2) improves blood glucose regulation,(3) achieves better weight management over time,(4,5) and lowers the risk of certain types of cancer.(6) A critical appraisal of the body of evidence is reflected in multiple national dietary guidelines that inform the community to eat more "grain foods particularly whole grain cereals" and to reduce consumption of refined grains.(2,7)

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Color versions of one or more of the figures in the article can be found online at www.tandfonline.com/lfri.

Sorghum (*Sorghum bicolor* (L.) Moench) is an example of a so-called ancient whole grain cereal that is better known to Western societies as an animal feed rather than a human food source. Sorghum is grown around the world, and ranks fifth in global cereal production, after maize, rice, wheat, and barley.(8) In many countries of Africa, Asia, and Central America, sorghum is widely cultivated due to its adaptability to semiarid and arid conditions and high temperatures. In these regions it is a major contributor to the staple diets of local populations.(9) In countries such as Australia and the United States, the primary use of sorghum has been as livestock feed and more recently in biofuel production.(9) Increasingly, the nutritional and agronomic advantages of sorghum, combined with a growing consumer movement dedicated to "healthy living," has peaked commercial interests in developed economies on how to make sorghum-based food products more accessible to consumers who remain largely unaware of their potential health benefits.

The starting point for exposing health benefits of foods is often their nutritional properties. In the case of sorghum, as with plant foods generally, the phytochemical component is of particular interest and this reflects recent developments in the nutritional sciences. The type of phytochemicals in some sorghum varieties have been purported to reduce the risk of certain types of cancer, cardiovascular disease, obesity, and diabetes.(10) Sorghum also has decreased starch and protein digestibility in vitro and is high in dietary fiber and resistant starch, and this array of qualities may play a role in mechanisms that reduce disease risk (Table 1(10−17)). Not least is the fact that sorghum is gluten-free and is suitable for people with celiac disease and other intolerances.(18)

Table 1
Sorghum's nutritional and functional attributes associated with metabolic disease effects

Component/property	Proposed benefits
Slow starch digestibility(11,12) (slowly digestible starches; interactions with endosperm and polyphenolic compounds that reduce starch hydrolysis)	Potential to attenuate blood glucose and insulin responses and increase satiety through reduction of glycemic index of sorghum-based foods. This has relevance in appetite regulation, weight management, and risk reduction of obesity-related diseases such as diabetes.
High antioxidant activity(10) (phenolic acids, monomeric polyphenolic flavonoids, polymeric polyphenolic condensed tannins)	Potential to reduce oxidative stress that plays an important role in the pathogenesis of many chronic diseases such as diabetes, atherosclerosis, some cancers, aging, arthritis, and neurological diseases
High fiber(13) (including resistant starch, ranging from 2.2 g(14) to 6.5 g(15) per 100 g dry matter)	Offers benefits to gut microbiome, metabolic disease risk, and gastrointestinal health
High unsaturated fatty acid content of lipid(16) (oleic acid, linoleic acid, linolenic acid, and policosanols in wax(17))	Improving dyslipidemia and thus promoting heart health

In a traditional nutrition sense, the value of sorghum grain has been considered to be slightly inferior compared with other cereal grains on the basis of lower protein and starch digestibility and, consequently, reduced metabolizable energy. This consideration is especially relevant to many of the world's poorest and most food-insecure communities where sorghum is a core food. In these cases, sorghum is combined with legumes and other cereals to increase macro- and micronutrient density of sorghum-based foods and diets,[19,20] and biofortified transgenic sorghum lines have been developed.[21] Paradoxically, these properties of lower digestibility and reduced available energy may prove to be better suited in populations where overweight- and obesity-related chronic diseases, such as metabolic syndrome, diabetes, heart disease, and cancer, are major public health issues.[22]

Over the past decade, Awika and Rooney,[10] Dicko et al.,[23] and Taylor and Emmambux[24] have exposed the potential role of sorghum in human health and in disease prevention. They have argued for a paradigm shift from perceiving sorghum as a low-value cereal grain to a health-promoting, environmentally sustainable food for inclusion in the global human diet. In order to achieve commercial adoption of this position, food innovation is required that would extend the range of sorghum-based products available to consumers. At the same time, quality human clinical trials are required to provide evidence of effects.

The research needs to be conducted in a food-health paradigm that considers not only the effects of individual grain constituents and their involvement in physiological processes, but also the effects of consuming sorghum-based foods within the broader context of whole diets. Because sorghum has been largely used as an animal feed in Western societies, much of the research has been done on livestock, but a wide range of studies have emerged that provide the basis for moving into human clinical studies. With this backdrop, the aims of this paper are to (1) provide a general overview of sorghum components and the related mechanisms of action that may impact on health and (2) provide a narrative review of the scientific evidence for effects of sorghum consumption on health outcomes.

Nutritional and Chemical Composition of the Sorghum Grain

Sorghum is a self-pollinating, summer plant belonging to the grass family of Poaceae. Sorghum grain is similar to maize with respect to chemical composition, with its key components being starch, proteins, lipids, nonstarch polysaccharides, and phytochemicals such as phenolic compounds, phytosterols, and policosanols. Sorghum grain also contains dietary fiber, including resistant starch, and micronutrients including vitamins and minerals, oil bodies, and waxes.

The proximate nutritional composition of sorghum whole grain is similar to wheat whole grain; energy density is 1377 vs. 1418 kJ/100 g dry weight, total carbohydrate 74.6 vs. 71.1, fat 3.3 vs. 2.5, and protein 11.3 vs. 13.7 g/100 g dry weight, respectively (Table 2[25,26]). However, sorghum has lower starch digestibility relative to other grains such as maize, rice, wheat, and barley, although the degree of digestibility depends on the method of processing.[11,27] The nutritional quality of sorghum proteins is diminished because they are more resistant to digestion[27] and have low levels of essential amino acids such as lysine, tryptophan, and threonine.[28] In contrast, there are high levels of leucine that were previously implicated, but now not accepted, as a cause of niacin deficiency and consequently endemic pellagra in some sorghum-eating populations.[29–32]

Table 2
Nutritional composition of sorghum, wheat, and corn (per 100 g dry weight, edible portion)[25,26]

Nutrient	Sorghum, white, whole	Wheat, durum, whole	Corn, yellow
Proximates			
Energy (kcal/kJ)	329/1377	339/1418	365/1527
Protein (g)	10.62	13.68	9.42
Total lipid (fat) (g)	3.46	2.47	4.74
Carbohydrate, by difference (g)	72.09	71.13	74.26
Fiber (g)	6.7#	10.7*	7.3
Lipids			
Fatty acids, total saturated (g)	0.610	0.454	0.667
Fatty acids, total monounsaturated (g)	1.131	0.344	1.251
Fatty acids, total polyunsaturated (g)	1.558	0.978	2.163
Cholesterol (mg)	0	0	0
Minerals			
Calcium, Ca (mg)	13	34	7
Iron, Fe (mg)	3.36	3.52	2.71
Magnesium, Mg (mg)	165	144	127
Phosphorus, P (mg)	289	508	210
Potassium, K (mg)	363	431	287
Sodium, Na (mg)	2	2	35
Zinc, Zn (mg)	1.67	4.16	2.21
Copper, Cu (mg)	1.080	0.553	0.314
Manganese, Mn (mg)	1.630	3.012	0.485
Selenium, Se (mg)	12.2	89.4	15.5
Vitamins			
Vitamin C, total ascorbic acid (mg)	0	0	0
Thiamin, B_1 (mg)	0.332	0.419	0.385
Riboflavin, B_2 (mg)	0.096	0.121	0.201
Niacin, B_3 (mg)	3.688	6.738	3.627
Pantothenic acid, B_5 (mg)	1.250	0.935	0.424
Vitamin B_6 (mg)	0.440	0.419	0.622
Folate, DFE (μg)	20	43	19
Vitamin B_{12} (μg)	0	0	0
Vitamin A, RAE (μg)	0	0	11
Vitamin D (IU)	0	0	0
Vitamin E (α-tocopherol) (mg)	0.50	0.71*	0.49

(*Continued*)

Table 2
(Continued)

Nutrient	Sorghum, white, whole	Wheat, durum, whole	Corn, yellow
Amino acids			
Tryptophan (g)	0.124	0.176	0.067
Threonine (g)	0.346	0.366	0.354
Isoleucine (g)	0.433	0.533	0.337
Leucine (g)	1.491	0.934	1.155
Lysine (g)	0.229	0.303	0.265
Methionine (g)	0.169	0.221	0.197
Cystine (g)	0.127	0.286	0.170
Phenylalanine	0.546	0.681	0.463
Tyrosine (g)	0.321	0.357	0.383
Valine (g)	0.561	0.594	0.477
Arginine (g)	0.355	0.483	0.470
Histidine (g)	0.246	0.322	0.287
Alanine (g)	1.033	0.427	0.705
Aspartic acid (g)	0.743	0.617	0.655
Glutamic acid (g)	2.439	4.743	1.768
Glycine (g)	0.346	0.495	0.386
Proline (g)	0.852	1.459	0.822
Serine (g)	0.462	0.667	0.447

*Value is for whole grain wheat flour.
#Value is for white sorghum (fiber in other types of sorghum ranges from 8.8 to 11.1 g/100 g).

As with cereals more broadly, sorghum is a source of B-complex vitamins (such as thiamin, riboflavin, vitamin B_6, biotin, and niacin) that are diminished with grain refining processes, including decortication.(33) The mineral composition in sorghum is similar to millet, higher compared with maize but lower than wheat, and is predominantly composed of potassium and phosphorus (Table 2).(34) Sorghum-based foods are a good source of both iron and zinc, although antinutrients such as phytates may diminish bioavailability,(35,36) a problem not unique to sorghum but common to other grains and plant foods in general. A complete nutrient analysis of sorghum is detailed in Table 2.

Components of Sorghum with Potential for Functional Properties

Starches

Sorghum grain is a good source of starch, containing approximately 71% of dry whole grain weight.(26) The starch is encapsulated in granules that are located predominantly in the endosperm (storage tissue), although uniquely some are present in the pericarp (outer layer of grain).(26) Sorghum starch is composed of both amylose and amylopectin polysaccharides (branched polymers of glucose), with very low percentages of amylose present in the starch of waxy sorghum varieties compared with 24–33% in nonwaxy sorghum starch.[24] Sorghum starch granules are enmeshed in a strong protein matrix in the endosperm,[1] a unique structural aspect of sorghum grain.[27] Disulfide-bond cross-linking involving kafirins in the protein matrix forms a protective network around the starch granules, reducing starch digestibility.[12]

The lower starch digestibility reported for sorghum foods is not an intrinsic property of the sorghum starch granules themselves, but appears mainly to be a consequence of the interactions of the starch with the endosperm protein matrix, as well as with cell wall material and polyphenolic compounds, such as condensed tannins and flavonoids.[37–41] These interactions inhibit carbohydrate-hydrolyzing enzymes, such as α-glucosidase and α-amylase, thereby lowering starch digestibility.[42] The presence of the protein matrix has also been associated with reduced starch gelatinization during cooking, resulting in partially gelatinized sorghum starch granules that may resist enzymatic degradation in vivo.[27] Sorghum starch has amongst the highest gelatinization temperatures, ranging from 66 to 81 °C, depending upon cultivars, and is higher than that of maize, wheat, and barley.[24,43] However, the extent of gelatanization of starch granules as a result of processing cannot easily predict in vivo digestibility and physiological effects such as glycemic responses. Factors such as the precise ratios of amylose to amylopectin, their arrangement within the starch granule, further degradation of other polymer molecules, and postprocessing conditions also influence the postprandial effects of a starchy food.[44]

Recent publications report on the in vitro starch digestibility of different sorghum foods, including sorghum-refined maize snack-like extrudates,[45] whole grain sorghum-refined wheat flour flat bread,[46] and whole grain sorghum-durum semolina pasta.[14] These in vitro studies confirm that sorghum foods can be formulated and processed to deliver slowly digested starch (SDS), with the potential to assist in improving blood glucose control; however, these predicted positive results require rigorous testing in humans.

Resistant Starch and Nonstarch Polysaccharides

Sorghum foods also contain varying amounts of resistant starch (RS), depending on factors such as processing, cooking, cooling, food storage, gelatinization, and cultivar.[14,15,40,46] Physiologically, RS resists hydrolysis by enzymatic digestion in the small intestine[47] and enters the colon where it is partially or completely fermented to produce beneficial short-chain fatty acids (SCFAs).[48] Here, the RS can act as a prebiotic[49,50] by stimulating the proliferation of beneficial bacteria already in residence in the gastrointestinal tract (GIT). To date, these effects have not been widely researched with respect to sorghum foods and sorghum-based diets.

Nonstarch polysaccharides (NSPs) have been associated with lower blood plasma cholesterol levels, reduced small intestine transit time, and improved bowel function.[51,52] NSPs are the major component of dietary fiber in sorghum grain and are mainly located in the pericarp and endosperm cell walls, constituting 2–7% of the total weight of the grain depending upon cultivar.[13,53] Sorghum NSPs are both cellulose and noncellulosic, consisting of arabinose, xylose, mannose, galactose, glucose, and uronic acid monomers.[24,54] The noncellulosic polysaccharides are primarily water-insoluble glucuronoarabinoxylans (GAX) along with β-glucans,[55] although naturally occurring β-glucans in sorghum are lower than that of barley and oats.[15,56] The GAX in sorghum are very abundant and are highly substituted with glucoronic acid residues, and acetyl and feruloyl compounds.

[1]Sorghum starch granules are densely packed in the *corneous endosperm* but exist in a more open structure in the *floury endosperm* of the grain caryopsis.

Sorghum contains other noncarbohydrate cell-wall components that form part of the dietary fiber fraction such as lignins, at levels up to 20% of the total cell wall contents by dry weight.(57) The total dietary fiber content of different sorghum cultivars ranges from 7.6% in low-tannin sorghums to 9.2% in high-tannin varieties,(13) and its level in sorghum-based meals can be manipulated by cooking and fermentation.(58) The effect of consumption of sorghum NSPs has not been investigated in humans.

Proteins

Protein is the second largest constituent of sorghum grain (6–18%) after starch.(59) Sorghum endosperm proteins are found in both a matrix and as protein bodies that are enveloped by the matrix. Sorghum proteins are classified as albumins, globulins, kafirins, cross-linked kafirins, and glutelins.(60) Of these, kafirins are the main protein,(61) constituting 50–70% of total protein content.(27) The kafirins are prolamin storage proteins with limiting levels of some amino acids, in particular lysine,(62) a disadvantage not unique among cereal grains. The kafirins differ in structure from the gliadin and glutenin storage proteins in wheat. They do not elicit damage to the mucosa of the small intestine of people with celiac disease,(18) making sorghum a viable ingredient for gluten-free foods such as bread. However, the inability of sorghum kafirins to make elastic dough and the difficulty in making bread of high consumer acceptability present challenges and have driven research into the manufacture of quality sorghum-based gluten-free food products.(46,63)

Sorghum kafirins are poorly digested due to the formation of cross-linking, especially when moist cooked, resulting in protease resistance.(27) In vitro and animal studies have also shown that sorghum protein digestibility may be reduced by other protein-protein, protein-phenol, and carbohydrate-phenol complexes that have been identified.(54,64–66) Cornu and Delpeuch(67) reported that the nitrogen digestibility in humans on a diet of 80% sorghum decreased from 65.4% to 60.5% when the decorticated sorghum in the diet was replaced by whole grain sorghum, suggesting that higher fiber sorghum varieties may have lower protein digestibility. Rather than a fiber effect per se, this more likely relates to the higher polyphenol content that naturally occurs in whole grain sorghum and the resultant binding of phenols to dietary protein.(54) In sorghum-consuming communities, where protein malnutrition is an issue, efforts to increase protein digestibility are imperative and lactic acid fermentation, decortication, and extrusion have been shown to improve digestibility and consequent amino acid availability.(45,66,68)

Sorghum grain also contains a broad range of bioactive peptides, recently reviewed by Lin et al.(69) These are of current interest to researchers due to their potential biological role in human physiological processes, including pathogenesis. The peptide bioactivities include antioxidant, antihypertensive, anticancer, antimicrobial, and opioid activities as well as immunomodulatory and cholesterol-lowering effects. The specific bioactive peptides isolated in sorghum include but are not limited to amylase inhibitors,(70) protease inhibitors,(71) cationic peroxidase,(72) 2-kDa antiviral peptide,(73) and xylanase inhibitors.(69) To date, research linking cereal grains with potential bioactive peptide activity has been limited; however, there are more sorghum studies appearing in the literature.(69,74) Overall, there is much to consider in translating this knowledge to human clinical trials, in particular the study populations of interest and the health/disease outcomes that might be researched.

Lipids

Sorghum grain contains approximately 3–4% lipids, the majority of which are neutral triglycerides, rich in unsaturated fatty acids, and mostly present in the germ.(16) The predominant fatty acids are oleic acid (31.1–48.9%), linoleic acids (27.6–50.7%), linolenic acid (1.7–3.9%), stearic acid (1.1–2.6%), palmitic acid (11.7–20.2%), and palmitoleic acid (0.4–0.6%).(26,75,76) Two less common saturated fatty acids, octanedioic (C8:0) and azelaic acid (C9:0), have been identified in some sorghum varieties.(75) This lipid composition has generated interest in sorghum as a source of edible oil, representing a potentially valuable dietary source of monounsaturated fatty acids (MUFAs) and polyunsaturated fatty acids (PUFAs), with higher PUFA levels than MUFA.(75) This desirable lipid composition is conducive to mechanisms that lower lipid levels in humans and therefore to potentially lower risk factors associated with heart disease.

Based on research in hamsters, Carr et al.(77) suggested that the primary cholesterol-lowering mechanism of sorghum lipid extracts appears to be a reduction in cholesterol absorption with a concomitant increase in fecal sterol excretion. Specifically, policosanols (a mixture of long-chain primary alcohols) in the sorghum lipid extracts appear to inhibit endogenous cholesterol synthesis.(77) Sorghum also contains plant sterols that may reduce cholesterol absorption to collectively lower plasma and liver cholesterol concentrations.(77) These results were recently supported by Lee et al.(78) in a hamster model of hypercholesterolemia, investigating the effects of whole kernel grain sorghum oil (rich in plant sterols) and wax (high in policosanols). The authors report that the sorghum oil played a more significant role in modulating cholesterol, most likely by inhibiting absorption; however, subtle interactions by the wax may have contributed to the effect.(78)

The policosanols in sorghum wax (found on the surface of the grain kernel) are composed of mainly docosanol (C22), tetracosanol (C24), hexacosanol (C26), octacosanol (C28), triacontanol (C30), and dotriacontanol (C32).(79) In sorghum, C28 and C30 are the most abundant policosanols.(17) A mixture of C28 and C30 from sugar cane wax has been shown to improve blood lipid levels(80); however, reports on the human effects of sorghum-derived policosanols have not been published to date.

An alternative mechanism for the cholesterol-lowering effect of sorghum lipid extract was reported by Martinez et al.(81) from research done with hamsters. They reported that sorghum lipid extract acts as a "prebiotic" to improve the host cholesterol metabolism through effects on gut microbiota. *Bifidobacteria* significantly increased in the hamsters fed grain sorghum lipid extract and was positively associated with high-density lipoprotein (HDL) plasma cholesterol levels.(81) In humans, this shift in *bifidobacteria* is associated with improved overall health, including reduced gut infections and suppression of colon cancer initiation.(82–84)

Finally, sorghum lipids may also possess antiploriferation properties. Zbasnik et al.(85) extracted lipids from sorghum dry distiller's grain (a by-product of the ethanol industry) and observed an antiproliferative effect on human colon carcinoma cells. They suggested that the effect may have been a result of synergistic interactions of vitamin E (predominantly γ-tocopherol), triacylglycerides, free fatty acids (predominantly linoleic acid), policosanols, aldehydes, and sterols (predominantly campesterol and stigmasterol) that were identified in the extracts.(85) Although sorghum dry distiller's grain is primarily used for animal feed, it is chemically and microbiologically safe as a human food ingredient; therefore, further research in humans is relevant.

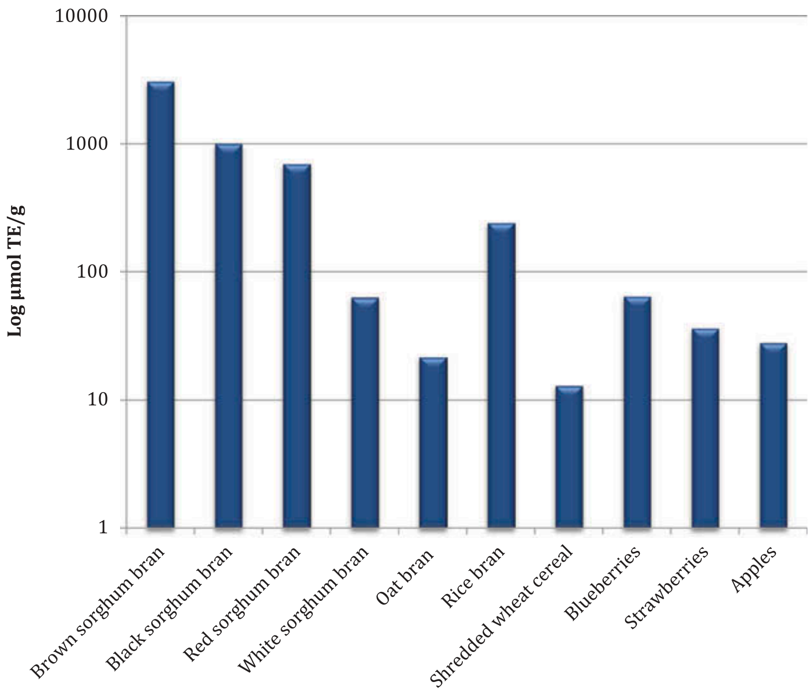

Figure 1. Antioxidant activity in sorghum bran fractions (dry basis) relative to other cereals and common fruits measured by oxygen radical absorbance capacity (ORAC) and expressed as µmol tocopherol equivalents (TE). Compiled from previously reported data.(10,25)

Phytochemicals

Most sorghum varieties, except white sorghums, have a high concentration of phytochemicals, particularly phenolic compounds, which exhibit high antioxidant activity and are linked to health benefits.(10,86,87) In fact, bran of some sorghum grain varieties reportedly has the highest antioxidant activity of all cereal crop fractions, even higher than many fruits and vegetables.(10) Specifically, sorghum bran has up to 2 orders of magnitude higher antioxidant activity than oat bran and wheat cereal, and an order of magnitude higher than rice bran although the precise amount is highly dependent on the variety of sorghum (Fig. 1(10,25)).

Phenolic compounds. The phenolic compounds in some sorghum grain varieties are more abundant and diverse than in any other cereal grain.(88) Sorghum grain varieties that have a pigmented testa and thick pericarps have the highest levels.(89) The phenolic compounds are concentrated in the bran component of the grain (in particular the testa and pericarp) and can be categorized into three main groups: (1) phenolic acids (hydrobenzoic acids and hydrocinnamic acids); (2) monomeric polyphenolic flavonoids (flavanols, flavanones, flavones, flavan-4-ols, and anthocyanins); and (3) polymeric polyphenolic condensed tannins (also known as proanthocyanidins or procyanidins).

The phenolic compounds in sorghum grain exhibit high antioxidant activity through their ability to scavenge free radicals.(88) The degree of antioxidant activity is correlated to the content of phenolic compounds in a specific sorghum cultivar, and this in turn is influenced by its genotype and growing environment.(89) Levels of phenolic compounds and the activity of enzymes that synthesize or catabolize phenols in sorghum grain strongly influence food product properties such as flavor and color and are therefore important determinants of sorghum for food use.(23) In general, sorghum processing decreases antioxidant activity, mainly as a result of reducing levels of measurable phenolic compounds.(90−92) This may be as a result of thermal degradation or lowered extractability during the analytical procedures used for their measurement.(91) However, some processes, including steeping, germination, fermentation,(93) and roasting of steamed grain,(94) have been reported to increase the level of polyphenolics. These may be related to improved extractability through breakdown of the food matrix, which might also result in higher bioavailability.

It has been postulated that sorghum grain phytochemicals may provide overall disease protection in vivo through not only antioxidative but also hypoglycemic and hypolipidemic mechanisms.(95,96) However, the extent of these health beneficial effects is unclear, since only limited clinical research has been reported. Reduction in oxidative stress is implicated in these protective processes(97); therefore, sorghum polyphenolic compounds may be relevant in disrupting the cascade of pathophysiological changes that lead to metabolic disease. In vitro, sorghum bran extracts with a high phenolic content and thus high antioxidant properties were shown to inhibit albumin glycation, whereas wheat, rice, oat, and low-phenolic sorghum bran extracts (such as white sorghum) did not.(98) Albumin glycation is the nonenzymatic process that results in formation of advanced glycation end-products (AGEs). AGEs have been associated with metabolic diseases such as diabetes and atherosclerosis. Human clinical investigations are warranted to further test these effects in vivo, especially since sorghum bran extracts have been suggested for use in food ingredients, food supplements, or nutraceutical products.

Flavonoids. The anthocyanin flavonoids found in pigmented sorghums, but not in white sorghums, are of particular interest to researchers, since some are unique to sorghum grain and they have potent antioxidant properties.(99) The 3-deoxyanthocyanins (3-DAs and derivatives) are the major class of flavonoid and are located in the pericarp.(88,100) 3-DAs lack the hydroxyl group in the 3-position of the C-ring and include the apigenidin and luteolinidin that are largely responsible for the pigmentation of certain sorghum grain varieties, namely, red and black sorghums.(101) A recent in vitro analysis of red sorghum flour extracts showed strong free radical scavenging activity as measured by an oxygen radical absorbance capacity (ORAC) assay and protection against low-density lipoprotein (LDL) oxidation, contributing to the evidence base for the potential of red sorghum as a valuable health-promoting food grain.(102) However, understanding the bioavailability of sorghum anthocyanins for the putative health-promoting effects in humans is a much-needed focus of future research.

In vitro research investigating effects of specific sorghum anthocyanins is emerging. A study utilizing the human epithelial larynx carcinoma cell line (Hep-2) by Devi et al.(103) demonstrated that anthocyanins extracted from red sorghum bran, specifically luteolinidin and apigenindin, induced significant antiproliferative activity. Powerful antiproliferative effects were also observed against colon cancer cells when black, red, and white sorghum extracts, rich in 3-DAs, were tested.(104,105) Yang et al.(106) proposed that these protective effects result from estrogen-induced apoptosis of the nonmalignant colonocytes that were strongly influenced by the flavones, apigenin, and luteolin. In breast cancer cell lines, 3-DAs isolated from red sorghum bran have been shown to have strong antiproliferative properties and to be cytotoxic.(107) Sorghum chloroform extracts have particularly strong anti-inflammatory effects in vitro (in both cell-free and cell-mediated experimental systems) through almost complete suppression of lipopolysaccharide-mediated production of nitric oxide, tumor necrosis factor-α, and interleukin-6. These effects are correlated to flavonoid concentration in the extracts.(108)

Tannins. Tannin sorghums contain high-molecular-weight *condensed tannins* that are oligomers or polymers composed of flavan-3-ol nuclei, found in the pigmented testa of the sorghum grain.(109) Condensed tannins exhibit strong antioxidant activity in vitro via free radical scavenging activity, chelation of transition metals, and inhibition of pro-oxidative enzymes. The antioxidant activity of sorghum tannins is higher than that of tannins extracted from any other crop.(88,99,110) In animal studies, sorghum tannins have been shown to be 15–30-fold more effective at quenching peroxyl radicals than simple phenolics.(111)

The presence of tannins in sorghum grain may reduce the nutritive value and lower metabolizable energy of the grain. Several mechanisms have been proposed to explain this "antinutritional" effect as reviewed by Awika and Rooney.(10) These include binding of proteins and carbohydrates into insoluble complexes that resist digestive enzyme breakdown(112−115); binding of digestive enzymes directly, inhibiting their enzymatic activity(116,117); and inhibition of intestinal brush border bound amino acid transporters,(118) particularly by tannin sorghums with higher degrees of polymerization,(119) resulting in reduced digestive enzyme activity. These effects were also reflected in animal feeding trials that demonstrated the feeding efficiency of tannin sorghums was 5–10% lower than non-tannin sorghums, depending on the animal species, the method of grain processing, and diet type. In general, animals consumed more feed yet experienced the same or slightly less weight gain when tannin sorghum formed the basis of their diets.(116,117,120) Such effects in a Western diet, where food is ubiquitous, may be beneficial if these results are to be translatable to humans.

Antioxidant tannins may be key protective components in sorghum foods for the mitigation of oxidative stress-induced diseases, with antiproliferative and anti-inflammatory effects as their key mechanisms of action. For example, brans from tannin sorghum varieties (naturally high in tannins, such as brown sorghum) and nontannin sorghum varieties (black-, red-, and white-grained) have demonstrated significant anti-inflammatory potential in vitro on the basis of strong inhibition of hyaluronidase activity (enzymes involved in cancer metastasis, osteoarthritis and skin aging).(121) The inhibition of the hyaluronidases correlated positively with total phenolic content and antioxidant capacity of the extracts, with greater effects observed in sorghum bran extracts than those of wheat and rice bran. In two experimental inflammatory systems using blood cells and a mouse model, Burdette et al.(122) also demonstrated that the anti-inflammatory activity of ethanolic extracts of different sorghum brans correlated with their phenolic content and antioxidant activity. At present, it is not possible to extrapolate these in vitro effects to in vivo effects after realistic consumption of sorghum by humans. However, the research provides mechanistic models for further investigation.

Grimmer et al.(123) demonstrated the potent antimutagenic activity of higher molecular weight compared with lower-molecular-weight tannins isolated in sorghum-derived polyphenol extracts. Gomez-Cordoves et al.(124) also demonstrated that sorghum tannins induce anticarcinogenic effects against human melanoma cells in vitro through increased melanogenic activity (a protective effect against ultraviolet [UV] irradiation damage to human skin) and therefore reduced formation of human melanoma cells. Collectively, these cell line studies demonstrate the bioactive potency of sorghum grain constituents, in particular the tannins, although in vivo studies have not occurred.

Experimental Research on Sorghum Consumption

Despite the diversity of bioactive components in sorghum, human studies investigating specific effects of sorghum consumption on protective health benefits are severely limited. Although numerous studies have been conducted with human subjects (Table 3[19,29,35,58,67,125–153]), the majority have addressed micronutrient metabolism (such as interactions between leucine, molybdenum, and niacin),[129] iron absorption from cereals,[35] dietary fiber effects,[140] protein digestibility,[144] and oral rehydration therapies.[148] This review therefore summarizes the experimental evidence that suggests protective health effects of sorghum consumption, targeting studies that investigate effects on energy balance, glycemic control, lipids, oxidative stress, and cell-mediated responses.

Effects on Energy Balance

Sorghum may be a valuable lower-calorie grain alternative in Western diets where overweight and obesity rates continue to rise and represent major public health burdens.[22] Sorghum's energy value is approximately 1377 kJ/100 g; however, the available energy for human metabolism may be lower than this estimate due to the described low starch and protein digestibility rates. This postulation is partly based on evidence from numerous feeding studies that show animals (from rodents to livestock species) fed whole grain sorghum, in particular the slowly digested high-tannin sorghum varieties, have reduced weight gain.[116,117,120,154,155]

In general, dietary fiber and whole grain intakes have been associated with reduced risks of obesity and overweight and with lowered waist-to-hip ratio.[156,157] Effects of dietary fiber on appetite and satiety have been proposed as major mechanisms for these reductions. Whole grain sorghum, with high fiber and slowly digestible starches, may increase satiety in humans due, in part, to effects on glycemic index of foods. It is believed that many communities in Africa who prefer to eat foods made from tannin sorghums do so because they impart stronger feelings of satiety and satiation compared with other cereals.[10] Sorghum's satiety effects in humans have not yet been investigated through controlled dietary trials.

Sorghum contains resistant starch (RS), and fermentation of RS in the colon is linked to a number of positive effects, including those on the gut microbiome.[50,158] Studies specific to energy control with sorghum intake are limited; however, a recent study by Shen et al.[159] evaluated the effects of sorghum RS on changes to body weight, blood lipids, and intestinal flora in 60 overweight and obese rats receiving treatment for 8 weeks. Results demonstrated that overweight rats fed a high-fat diet containing 30% sorghum RS gained less weight than rats fed a comparator diet devoid of sorghum RS ($P < 0.05$). However, there was no significant difference ($P > 0.05$) in weight measures in the obese rats that were administered the same test diets. Thus, sorghum RS did not overcome weight gain caused by high-fat diets, but it did have an ameliorating effect. Significant changes ($P < 0.05$) to the synthesis and secretion of serum leptin and adiponectin, two adipose-derived hormones that are involved in the regulation of food intake and body weight, were also reported in the sorghum RS groups, as were improvements to the intestinal flora ($P < 0.05$) (as measured by increased populations of *Bifidobacterium* and *Lactobacillus* and reduced populations of *Enterobacteriaceae*). This is an important study that demonstrates mechanisms by which

Table 3
Human studies incorporating sorghum-based test meals

Lead author/Year	Focus of investigations	Subjects/Experiment	Results
Nutrient and vitamin metabolism			
Gopalan et al. (1960)[29]	Role of amino acid imbalance (relative excess of leucine) in the pathogenesis of pellagra.	13 healthy and pellagrin subjects. 5 g dietary leucine administered daily and changes in urinary excretion of *N*-methyl nicotinamide (NMN) measured.	Leucine increased urinary excretion of NMN in all subjects. Isocaloric replacement of rice by sorghum (Jowar) resulted in increased urinary NMN excretion in all patients.
Deosthale et al. (1974)[125]	Sorghum molybdenum (Mo) consumption effects on copper (Cu) and uric acid excretion.	4 adult males (age not specified). Low (0.21 μg/g) and high (1.39 μg/g) Mo-containing grains were used in diets controlled for calories, protein, minerals, sulfur.	Uric acid increased only in high Mo intakes (10–15 mg Mo/day). Urinary Cu excretion was significantly increased with increasing levels of Mo. Fecal Cu excretion was unchanged.
Krishnaswamy et al. (1976)[126]	Vitamin B_6, leucine absorption.	6 healthy males (25–35 years). Metabolic interrelations between excess dietary leucine and vitamin B_6 studied.	Vitamin B_6 counteracted effects of leucine on urinary quinolinic acid excretion, in vitro nicotinamide nucleotide synthesis by erythrocytes; corrected abnormalities of 5-hydroxytryptamine metabolism induced by excess leucine.
Obizoba (1979)[127]	Mineral and vitamin metabolism.	5 healthy women (19–25 years). Fed 4 *iso*-nitrogeneous mixed plant protein diets various blends based on whole wheat, navy bean, and 3 sorghum flour varieties (Purdue normal, high lysine, and Nigeria normal).	Various effects on measured Ca, Mg, Fe, Niacin, riboflavin, and folic acid levels were reported and related to the contents in the test diet.

(*Continued*)

Table 3
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Lead author/Year	Focus of investigations	Subjects/Experiment	Results
Wang et al. (1991)[128]	Fiber effects on niacin status/niacin utilization.	10 healthy adult subjects. 28 g per day of ready-to-eat cereal (whole-ground sorghum flour) or cereal from decorticated sorghum flour (bran removed, polished). Urine, stool, and fasting blood samples collected.	Whole grain sorghum cereal decreased fecal transit time, lowered urinary NMN excretions, but raised blood serum levels of NMN and nicotinamide when compared with polished grain sorghum cereal.
Schmid et al. (2007)[129]	Dietary intake analysis of mothers and their children in South India.	218 mothers (>15 years) and their children (<5 years) in South India. Comparison of dietary intake of subjects with and without intervention to manage malnutrition.	Mothers had significant higher intakes of energy and protein in summer, and significant higher intakes of energy, protein, and Fe in rainy season. No differences in children. In mothers, sorghum contributed 29% energy, 33% protein, and 53% iron.
Iron (Fe) status/absorption			
Derman et al. (1980)[130]	Fe absorption from maize and sorghum.	21 male and female South African subjects, healthy and Fe deficient. Ages not specified. Study compared thin gruel, sorghum, and wheat beers.	Ten times as much Fe was absorbed from the traditional maize and sorghum beer as from gruel made from the same ingredients.

Radhakrishnan et al. (1980)[131]	Fe bioavailability.	12 healthy and 13 anemic subjects. Ages not specified. Diets based on high- and low-tannin sorghum.	In 12 healthy subjects, Fe absorption from the low- and high-tannin varieties was similar. In 6 anemic subjects, Fe absorption from low-tannin sorghum was significant higher. In the other 7 anemic subjects, there was no difference observed.
Gillooly et al. (1984)[132]	Fe absorption.	53 Fe-deficient Indian females (age not specified). 6 different experiments. Systematically examined effects on Fe absorption of polyphenol and phytate in sorghum.	When amounts of both compounds were reduced to low levels by pearling, there was a significant increase in Fe absorption.
Haidar et al. (1999)[133]	Fe deficiency anemia (IDA) status.	1449 pregnant and lactating subjects (15–49 years) in Ethiopia.	Overall status of IDA determined by hemoglobin level was 18.4 % with higher rates in maize, milk, and sorghum staple areas.
Hurrell et al. (2003)[35]	Fe absorption.	34 males and 44 females (21–38 years). Measured the influence of phytic acid degradation on Fe absorption from cereal porridges.	Phytate degradation improves Fe absorption from cereal porridges prepared with water but not with milk, except from high-tannin sorghum.

(*Continued*)

Table 3
(Continued)

Lead author/Year	Focus of investigations	Subjects/Experiment	Results
Cardiovascular effects			
Suhasini et al. (1991)[134]	Effect of unrefined sorghum or maize on serum lipids.	6 males and 10 females (23–26 years). Group 1 ate 100 g unrefined sorghum. Group 2 ate 50 g of unrefined maize.	Both diets showed significant reduction in serum total cholesterol and triglyceride levels with simultaneous increase in HDL cholesterol value over 3 weeks.
Diabetes/glycemia/oxidative stress research			
Mani et al. (1993)[135]	Determination of glycemic index of commonly consumed foods in India.	36 subjects (type 2 DM). Glucose responses were measured 1 and 2 hours after consumption of test foods (50 g available carbohydrate) and compared with a 50-g glucose load. 6 foods tested, 1 based on sorghum.	The mean glycemic index of the sorghum meal was 77% ± 8% (SE), indicating a relatively high glycemic index. No significant difference was observed in blood glucose level at the 1- and 2-hour time points when compared with the corresponding reference.
Lakshmi et al. (1996)[136]	Glucose and insulin responses to sorghum-based meals.	3 males and 3 females with type 2 DM (45–60 years). Consumption of whole grain sorghum meals compared with the same meals based on dehulled sorghum and other recipes prepared with wheat and rice.	The consumption of whole grain meals resulted in significant lower glycemic responses ($P <$ 0.05) in 6 subjects, in part due to differences in fiber content and cooking methods.

Abdelgadir et al. (2005)[137]	Glucose and insulin responses to 6 traditional Sudanese meals from wheat, sorghum, millet, and maize flours.	Glucose and insulin responses in a randomized crossover design with 10 subjects with type 2 diabetes mellitus (6 males and 4 females).	Millet porridge had the lowest postprandial glucose and insulin responses, followed by wheat pancakes, sorghum porridge, and sorghum flat bread. Maize porridge induced higher glucose and insulin responses (as measured by mean iAUC).
Poquette et al. (2013)[138]	Glucose and insulin responses to sorghum-based meals.	Randomized crossover design, 10 males consumed muffins containing 50 g of total starch from either grain sorghum flour or whole wheat flour. Plasma glucose and insulin measured over 3 hours.	Plasma glucose and insulin iAUC reduced by ~26% and 55%, respectively. Glucose and insulin measures were significantly lower for the sorghum muffins ($P < 0.05$) at different time points.
Khan et al. (2014)[139]	Plasma total polyphenols, antioxidant capacity, and oxidative stress responses to sorghum pasta meal.	Randomized crossover design, 22 males and females consumed pasta containing red or white whole grain sorghum flour (30% sorghum, 70% semolina) or a wheat control made from 100% semolina. One blood collection at 2-hour time point.	Plasma polyphenols, antioxidant capacity and superoxide dismutase (SOD) activity were significantly ($P < 0.001$) higher following red sorghum pasta (RSP) meal and protein carbonyl level was significantly lower ($P = 0.035$) following consumption of the RSP meal than the control meal (wheat).

(*Continued*)

Table 3
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Lead author/Year	Focus of investigations	Subjects/Experiment	Results
Specific fiber effects			
Cornu et al. (1981)(67)	Effect of fiber in sorghum on N digestibility.	12 healthy Cameroonian adult males whose habitual diet is based on a sorghum meal (2.4–4.2 g of crude fiber/100 g DM). Subjects received successive diets of 3.3, 4.8, and 5.4 g of crude fiber/100 g of DM.	Increased fiber intake resulted in a significant rise in quantity of fecal matter excreted (N and formic insoluble substances), but a reduction in urinary N losses.
MacLean et al. (1983)(58)	Effect of decortication and extrusion on the digestibility of sorghum.	9 children (7–24 months). Sorghum provided 8% protein and 62% carbohydrate (kCal) in diet. Lysine was supplemented to 3% of protein. Casein provided 6.4% protein (kCal) in the control diet.	N absorption from sorghum and control not different but N retention lower than control. Fecal weights and energy losses showed minor differences. Decortication and extrusion improve protein quality and digestibility of sorghum.
Fedail et al. (1984)(140)	Effect of sorghum and wheat bran on the colonic functions.	10 males (22–24 years) healthy Sudanese subjects. Comparative study of normal diet, diet of 20 g/day sorghum bran, and 20 g/day wheat bran, for 3 weeks. Wet stool weight, gut transit time, and frequency of bowel evacuation noted.	The mean stool weight on normal diet was 136.6 ± 43.1 g/day, on sorghum bran 173.3 ± 48.4 g/day, and on wheat bran 219.1 ± 98.3 g/day ($P < 0.001$). Both brans produced a similar number of bowel evacuations, stool weight, and transit time.

Cornu et al. (1986)[141]	Effects of fiber on digestibility of sorghum lipids.	12 healthy Cameroonian adult males whose habitual diet is based on a sorghum meal (2.4–4.2 g of crude fiber/100 g DM). Subjects received successive diets of 3.3 (A), 4.8 (B), and 5.4 (C) g crude fiber/100 g of DM.	Reduced lipid digestibility occurred in all diets. No difference was observed between A and B fiber diets but dropped with diet C. Lipid losses increased more rapidly than N losses with increasing fiber content. No significant changes in concentrations of fecal fat.
Protein digestibility			
Kurien et al. (1960)[142]	Metabolism of N, calcium, and phosphorus.	7 boys (10–11 years). Effect on metabolism of N, Ca, and P of replacing 25%, 50%, or 100% of rice in a poor Indian diet by *Sorghum vulgare* was studied. Daily intake of N was constant in all diets.	Protein digestibility coefficients of protein and mean daily N retention diminished as sorghum increased. Sorghum led to (1) higher Ca intake, but Ca retention decreased; and (2) higher P intake, which resulted in higher P retention.
Nicol et al. (1978)[143]	Utilization of protein in cassava, rice, and sorghum (*Sativa*)–based diets.	19 Nigerian men, 13 different feeding trials, each of 6 men. Net protein utilization (NPU) of diets based on rice, sorghum, or cassava was compared with a minimal protein diet. Endogenous N excretion measured.	The NPU of a diet based on home-pounded, winnowed sorghum flour was higher than that of a diet based on milled whole-meal sorghum due to the low digestibility of the latter diet.

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Lead author/Year	Focus of investigations	Subjects/Experiment	Results
MacLean et al. (1981)[144]	Protein quality and digestibility of sorghum.	13 children (6–30 months). Protein quality and digestibility of 2 high-lysine (2.9–3.0 g/100 g protein) and 2 conventional varieties (lysine content 2.1–2.2 g/100 g protein) of whole grain sorghum milled were assessed.	Weight loss or poor weight gain was reported. No difference by variety in N absorption or retention. Stool weight and energy loss 2.5–3× control values. Total concentration of essential amino acids was low, as were concentration Lys and Thr. Lys was the limiting amino acid.
Weaning or therapeutic foods			
Dibari et al. (2013)[145]	Acceptability/safety of new ready-to-use therapeutic foods (RUTF) before use.	41 HIV/TB patients (>18 years) in Kenya. Crossover RCT comparing soy/maize/sorghum RUTF (SMS-RUTFh) to control 10-day measures of product intake.	SMS-RUTFh is acceptable and can be safely clinically trialed, if close monitoring of vomiting and nausea is included.
Bisimwa et al. (2012)[146]	Fortified soybean-maize-sorghum paste vs. fortified corn soy blend porridge in underweight infants.	6-Month Congolese infants randomly assigned to lipid-based ready-to-use complementary foods (RUCF; n = 691) or fortified corn soy blend (UNIMIX, n = 692) for 6 months. Hemoglobin, triglyceride, and cholesterol noted.	No significant differences in the concentrations of hemoglobin, serum triglyceride, and serum cholesterol were found between the 2 groups.

Human oral rehydration solutions based on sorghum			
Mustafa et al. (1995)[147]	Oral rehydration therapy for acute diarrhea using cereal-based solutions.	96 Sudanese children aged 6–40 months. Comparative RCT (32 rice, 34 sorghum, 30 control). Safety and efficacy of rice or sorghum cereal-based oral rehydration solutions (ORS) relative to standard. WHO ORS formulation.	Cereal-based ORS shortened the duration of diarrhea, reduced stool volume, and the frequency of diarrhoea and vomiting, and the mean total ORS intake. These effects were more marked with the sorghum-based ORS than with the rice-based ORS.
Molla et al. (1989)[148]	Food-based oral rehydration solution (maize, millet, wheat, sorghum, rice, potato).	266 children (1–5 years), history of acute diarrhea for ≤48 hours. Digestibility of food-based ORS was assessed by stool pH, glucose content before and after acid hydrolysis and osmolality.	The mean stool output over the first 24 hours in standard ORT was significant higher than food-based ORT. Food-based ORT showed substantial reduction in stool output.
Pelleboer et al. (1990)[149]	Oral rehydration therapy for acute diarrhea.	64 Nigerian children (2.5 months–5 years). Comparative RCT—subjects consumed either the WHO recommended oral rehydration solution (WHO-ORS) or a solution, containing 60 g/L sorghum powder.	No significant differences in amt. of fluid used, number of stools, and duration of diarrhea. No significant difference in weight gain. 7 children died, 2 (6%) in the sorghum-ORS group and 5 (17%) in the WHO-ORS group. Sorghum-ORS was well accepted and tolerated.
Consumer/sensory/acceptability studies			
Kayitesi et al. (2010)[19]	Consumer opinions of marama/sorghum composite porridge.	30 males and 22 females. Descriptive sensory analysis, consumer testing, texture analysis, pasting and color.	The 100% sorghum porridge and the composite porridge with full-fat flour were the most acceptable to consumers.

(*Continued*)

Table 3
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Lead author/Year	Focus of investigations	Subjects/Experiment	Results
Vazquez-Araujo (2012)[150]	Consumer input for developing human food products made with sorghum.	Adults $n = 34$ focus groups; $n = 1002$ national survey; $n = 160$ conjoint analysis	Heath aspects of grain products were the most appealing for consumers, whereas conjoint analysis showed that sensory attributes were the principal drivers for purchase intent.
Muhihi et al. (2013)[151]	Sensory study: sorghum ugali (stiff porridge).	Overweight and obese Tanzanian adults. Pre-and posttesting questionnaires were administered. A 10-point Likert scale used to rate attributes of 3 test foods. Sorghum ugali was consumed by 23% of participants.	All of the test foods were highly rated for smell, taste, color, appearance, and texture. Taste was rated highest for unrefined maize ugali. Whole grain carbohydrates are highly acceptable.
Effects on immune status in people with HIV			
Motswagole et al. (2013)[152]	Effects of a sorghum meal on the immune status of adults with HIV.	132 HIV+ adults. Double-blind, randomized, placebo-controlled trial in Botswana. Micronutrient fortified sorghum meal including vitamin A ($n = 67$) or control ($n = 65$). Serum retinol, Fe, Zn, albumin, CD4 cell count and HIV viral load assessed over 12 months.	Fortified sorghum meal did not influence serum retinol, CD4 cell count, and HIV viral load.
Ayuba et al. (2014)[153]	Effects of supplementation with sorghum herbal preparation (Jobelyn) on immune status.	61 HIV+ adults in Nigeria—2 trials. 10 HIV+ patients not receiving antiretroviral therapy (ARVT). Patients consumed 500 mg Jobelyn daily for 8 weeks. Control with 51 HIV+ patients receiving ARVT.	Consumption of Jobelyn contributed to improved hemoglobin levels and increased CD4 cell counts HIV+ patients.

sorghum RS may assist in the prevention and treatment of obesity. The study also identified positive lipid changes. Triglycerides, total cholesterol, and LDL cholesterol in both the overweight and obese rats consuming sorghum RS–enriched diets were significantly lower than the control groups ($P < 0.05$). HDL-cholesterol levels were significantly higher in the sorghum RS groups ($P < 0.05$). It remains to be seen whether these effects can be translated to the human condition. At this stage, the human studies demonstrate only possible mechanisms, but the positive results in animal models identify that whole grain sorghum may be useful in managing energy balance to assist with control of overweight and obesity.

Effects on Glycemic Control

Sorghum foods have demonstrated slow starch digestibility in vitro and in animal feeding trials, suggesting favorable effects on postprandial glycemic and insulinemic responses in humans. Numerous animal feeding studies have shown that sorghum in the diet effectively improves glucose metabolism compared with sorghum-free diets.[111,160–162] A limitation in some of these studies is that the specific type of sorghum extract is not defined; thus, it cannot be determined whether effects are linked to phenolic, fiber, or macronutrient contents. Furthermore, whether the concentrations of sorghum extracts are physiologically relevant, that is, capable of eliciting these blood glucose attenuation effects in humans after a realistic dose, is not yet clear.

A recent study by Cervantes-Pahm et al.[163] reported on the use of a pig model to investigate the comparative nutrient and energy digestibility of a range of grains widely used for human consumption, including whole grain sorghum. In this study, the apparent ileal digestibility of sorghum starch was lower than for corn.[163] The authors attributed this to the high level of resistant starch in sorghum, which appeared to be fully fermented in the pig hindgut, since ∼100% starch disappearance was reported. The low apparent ileal digestibility of its starch in pigs suggests that sorghum may be of value for reducing the glycemic index of human foods.[163] Caution in extrapolating these pig trials to human health is needed, since in this study raw grains were used, whereas in human food the grains are invariably cooked, changing the structure and digestion properties of the starch.

Dixit et al.[164] have even gone as far as to specifically recommend sorghum grain be regularly consumed in the modern Indian diet to assist in the reduction of type 2 diabetes and cardiovascular disease in this population. Despite the positive recommendation, only four in vivo human studies exploring these effects have been reported in the literature, each with limitations and inconsistencies.[135–138] The most recent of these human studies investigated the effects of consuming muffins made from grain sorghum on plasma glucose and insulin levels.[138] In a randomized crossover design, 10 male subjects consumed muffins containing 50 g of total starch (TS) from either grain sorghum flour or whole wheat flour (although the available carbohydrate was not reported), with all additional ingredients the same across both treatments. Glucose and insulin levels were measured at baseline (15 minutes prior to consumption), time point 0 (onset of consumption) and 15, 30, 45, 60, 75, 90, 120, and 180 minutes after consumption. Additionally, levels of rapidly digestible starch (RDS), SDS, RS, and TS in muffins were analyzed. Results indicated that RDS, SDS, and RS contents were significantly higher in sorghum muffins compared with wheat muffins ($P < 0.05$). Plasma glucose incremental area under the curve (iAUC) reduced by ∼26%, and glucose measures at the 45–120-minute intervals were significantly lower for the sorghum muffin ($P < 0.05$). Also, plasma insulin iAUC reduced significantly, and insulin measures at the 15–90-minute intervals were significantly lower for the sorghum muffins ($P < 0.05$), reducing by ∼55%. Lack of information on the available carbohydrate in each test muffin is a limitation, but this study shows the potential of sorghum-based foods to attenuate blood glucose and insulin responses.

In a similar study, Lakshmi and Vimala[136] also demonstrated that the consumption of whole grain sorghum meals, compared with consumption of the same meals based on dehulled sorghum and other recipes prepared with wheat and rice (as controls), resulted in significantly lower glycemic responses ($P < 0.05$) in six subjects with type 2 diabetes mellitus.[136] These observations may have been in part due to the difference in fiber content of the meals that ranged from 2.2 to 4.8 g in whole grain sorghum treatment meals and 1.8 to 2.7 g in dehulled sorghum treatment meals. Also, the different cooking methods utilized in the treatment meal recipes (pan-fried, boiled, fermented-steamed) may have had an effect on starch digestibility and therefore carbohydrate metabolism.

Further glucose control studies by Mani et al.[135] evaluated the glycemic index (GI) of six traditional Indian meals, one of which was based on sorghum. The test meals were consumed as baked bread (prepared from flours of sorghum or finger millet or pearl millet) or as pressure-cooked meals (based on kodo millet, consumed as is or with added whole mung beans or with added mung bean dal). No fats were added in the preparation of the test meals. Testing was undertaken in 36 subjects with type 2 diabetes mellitus. Glucose responses were measured 1 and 2 hours after consumption of the test foods (50 g available carbohydrate) and compared with a 50-g glucose load. The mean GI of the sorghum bread was relatively high at 77% $\pm$ 8% (SE), but not as high as the finger millet bread, which had a GI of 104% $\pm$ 13% (SE), equivalent to the glucose load. The pearl millet bread had the lowest GI of all six test meals, producing a GI of 55% $\pm$ 13% (SE). No significant difference was observed in blood glucose level after each of the test foods at the 1- and 2-hour time points when compared with the corresponding blood glucose response to the 50-g glucose load. The study identifies sorghum's digestibility in this meal format (baked bread) may not be as slow as in vitro studies may suggest.

Abdelgadir et al.[137] investigated the influence of six traditional Sudanese carbohydrate-rich meals (prepared from wheat, sorghum, millet, and maize flours) on glucose and insulin responses in a randomized crossover design with 10 subjects with type 2 diabetes mellitus (6 males and 4 females). Millet porridge had the most favorable (lowest) postprandial glucose and insulin responses, followed by wheat pancakes, then sorghum porridge and sorghum flat bread, whereas maize porridge induced higher glucose and insulin responses (as measured by mean IAUCs). Consideration of the method and time of preparation, particularly the duration of fermentation and the degree of milling, as well as the nature of starch and fiber content is important when interpreting these findings. That is, inadequate reporting of the precise physicochemical properties of the final products limits generalizability in food studies. Overall, the glucose and insulin response studies using sorghum in humans have used small sample sizes with ambiguous results.

Effects on Serum Lipids

Mechanisms for the role of sorghum grain components in cardiovascular protection have been investigated.[10] Only one study has been conducted with human subjects (10 males and 6 females) to investigate the effects of consuming sorghum foods on serum lipid levels as an indicator of cardiovascular disease risk.[134] In this study, a significant reduction ($P <$ 0.05) in total cholesterol, triglycerides, and HDL cholesterol was observed after daily consumption of 100 g of unrefined sorghum in the form of pancakes over 3 weeks. However, the content of subjects' background diets was not adequately reported, making assessment of dietary confounders difficult.

Most of the research identifying beneficial effects of sorghum consumption still lies with animal models.[111,159,161,165–167] Klopfenstein et al.[168] concluded that sorghum bran was effective in lowering serum and liver cholesterol levels in hamsters. This effect was repeated in another hamster model of hypercholesterolemia, when grain sorghum lipid extract included in the diet significantly reduced plasma non-HDL and liver esterified cholesterol levels while increasing HDL levels.[77] In all these studies, total cholesterol levels were reduced in animals consuming sorghum-based diets compared with sorghum-free control diets. In a single negative finding, Lee et al.[169] found that although sorghum consumption increased HDL-cholesterol levels, total cholesterol and LDL-cholesterol levels were increased in a rat model. However, the lack of a control group in this research makes conclusions difficult.

Sorghum tannins have not been broadly investigated in relation to their effects on cardiovascular disease risk factors, unlike tannins from some other foods and beverages such as red wine and tea. There may be an anticoagulant effect of sorghum tannins, yet to be tested in humans, as evidenced in cultured mullet fish that were fed tannin-containing sorghum distillery residues.[170] The sorghum residue significantly improved blood thinning and erythrocyte membrane integrity of the fish blood cells in cooler water temperatures over the winter months, enabling normal blood viscosity and prevention of red blood cell hemolysis induced by typical oxidation processes. The authors suggest that the antioxidant activity of the tannins and polyphenols present in the sorghum residue contributed to the prevention of red blood cell hemolysis. A translation to human studies has yet to be conducted.

Effects on Oxidative Stress Biomarkers and Plasma Antioxidant Capacity

A randomized, controlled, crossover human study, involving 22 healthy adults, was conducted to assess the acute effects of consuming pasta containing red or white whole grain sorghum flour (30% sorghum, 70% semolina) on plasma total polyphenols, antioxidant capacity, and oxidative stress markers compared with a wheat control made from 100% semolina.[139] Compared with baseline, the 2-hour postprandial levels of plasma polyphenols, antioxidant capacity, and superoxide dismutase (SOD) activity were significantly ($P < 0.001$) higher following the red sorghum pasta (RSP) meal, whereas the protein carbonyl level was significantly lower ($P = 0.035$). Furthermore, net changes in polyphenols, antioxidant capacity, and SOD activity were significantly ($P < 0.001$) higher, whereas protein carbonyls were significantly ($P = 0.035$) lower following consumption of the RSP meal than the control meal. Pasta containing red whole grain sorghum flour, but not white sorghum flour, enhanced antioxidant status and improved markers of oxidative stress in healthy subjects. The increase in plasma polyphenols by the RSP meal may be attributed to its higher content of polyphenols. The potential limitations of this study include the short duration and use of only one postprandial blood collection. Furthermore, subjects in this study were healthy and their results may differ to people with oxidative-stress-induced disease such as diabetes and obesity. Studies in subjects with mild to moderate oxidative-stress-induced disease and who consume a sorghum-enriched diet daily over an extended period of time are required to further investigate potential antioxidant effects of sorghum consumption.

Effects on Cell-Mediated Immune Responses

Cell-mediated immune responses have been linked to cancer development. Epidemiological evidence dating back to the early 1980s has correlated consumption of sorghum with reduced incidence of esophageal cancer, warranting closer attention to the potential chemopreventive properties of sorghum chemical components. Data from various sorghum-consuming countries in Africa and Asia have demonstrated lower esophageal cancer incidences compared with regions where wheat and maize were the major cereals consumed.[171–174] However, contamination of maize in these communities by the *Fusarium* fungi, which convert nitrates to nitrites, known carcinogens, has been identified as a more likely cause of increased rates with maize consumption. Nevertheless, such epidemiological observations have driven research efforts towards understanding potential cell-mediated chemopreventive properties of sorghum grain components and their mechanisms of action not just against esophageal cancer, but other cancers of the gastrointestinal tract and beyond. Currently research is in its infancy, with growing numbers of cancer cell line studies exploring anti-inflammatory, antimutagenic, and antiproliferative effects that are important in prevention of carcinogenesis. Some animal studies have also shown that phenolic extracts derived from sorghum, on the basis of high antioxidant activity, particularly from red, black, and tannin sorghum varieties, have been able to effectively induce cell arrest and suppress tumor growth in vivo.[175,176] Many more in vitro and animal studies are required before antioxidant effects of sorghum extract, aimed at cancer prevention and treatment, can be justified in clinical trials. The role of sorghum consumption in cancer prevention is more likely to be examined in epidemiological studies, with mechanistic studies contributing to the discussion on the plausibility of findings.

Future Research Directions

A possible role for sorghum in prevention and treatment of metabolic disease requires greater investigation. Initial research would investigate acute responses such as blood glucose, insulin, and appetite responses to sorghum consumption. In vitro inhibition of glucose release by sorghum extracts (bran, phenolic, and lipid extracts) and a small number of human studies have demonstrated a lower glycemic response to sorghum-based foods; however, results were inconsistent. Sorghum's lipid profile, rich in unsaturated fatty acids, may provide additional lipid-lowering effects. As a fiber-rich food, sorghum is likely to impart satiating qualities. Specifically, designing studies that combine objective measures (physiological effects such as glucose, insulin, appetite hormones) with subjective analysis of appetite utilizing visual analogue scales (questions about hunger, desire to eat, satisfaction, fullness, and subsequent food intake) are important.[177] It is also important to consider that for functional foods to deliver their potentially subtle benefits, repeated consumption is required.[178]

Substantiating potentially beneficial effects of sorghum foods on chronic lifestyle-related disease risk factors requires rigorous scientific investigation in human studies whereby consistent results from randomized controlled trial (RCTs) are reported, contributing to the highest level of evidence for practice.[179] To date, there appears to be fewer than five RCTs investigating sorghum metabolic disease-related effects in humans, and all interventions are short term and have some experimental design shortcomings. Future RCTs should aim to directly examine a specific effect on chronic disease biomarkers or health outcomes between a control and sorghum-intervention diet, for a minimum of 3–6 months, enabling evidence for longer-term effects to emerge.[180] Specifically, studies should investigate lipid profiles, longer-term markers of glycemic control, and body weight. Although much of the research to date focuses on extracts and components, the impact of the whole food reflecting the synergy between the components needs to be considered. It is also important to study the content of the background diet in these RCTs as background diet can confound results and may interfere with the ability to attribute effects to the dietary variable of interest.(180) In addition, for translation to practice, the impact of sorghum-based foods on chronic lifestyle-related disease must be seen in the context of the whole diet, carefully monitored throughout trials.

The evidence for a relationship between the antioxidant activity of sorghum and health benefits of its consumption is of particular importance due to the role oxidative stress plays in chronic disease development. To date, several in vitro and animal model studies have highlighted the potential of sorghum grain components, such as polyphenols, to scavenge free radicals.(176,181−184) Unfortunately, these studies are limited in their ability to attribute direct antioxidant effects of sorghum, as they do not account for metabolic transformations and interactions that influence bioavailability and biological activity of the polyphenols in the body after ingestion. For example, it is unclear what transformations polyphenols undergo in vivo, from the oral cavity, through the gastrointestinal tract, and after absorption and metabolism.(185) Thus, test regimens from such in vitro and animal studies need to be repeated in humans with mild to moderate oxidative-stress-induced disease. Disease indicators, such as oxidative stress and inflammatory markers, can be measured in subjects who consume a sorghum-enriched diet daily over an extended period of time.

Finally, although the development of an evidence base for a link between sorghum consumption and chemoprevention is in its infancy, some evidence for strong antioxidant and anti-inflammatory effects that may mitigate cell proliferation, mutagenesis, and carcinogenesis has been reported. Cell line and animal studies have demonstrated the potential for such cell-mediated effects but require substantiation in humans. Determining whether the concentration of sorghum grain extracts used in these studies may be feasibly consumed through dietary intake of sorghum-based foods is critical. Notwithstanding, the study of food effects on cancer is highly complex and clinical trials are problematic for ethical reasons. Even so, knowledge generated through various forms of experimental research adds to a general understanding of how the sorghum food matrix may be beneficial.

Conclusions

There is an emerging body of scientific literature on sorghum (*Sorghum bicolor*) as an underutilized cereal whole grain that may contribute to the prevention of chronic lifestyle-related diseases, particularly in regions where associated morbidity and mortality rates are significant public health burdens.(22) This review identifies that sorghum grain components may have an impact on metabolic disease processes through the delivery of slowly digestible starches, resistant starch, dietary fiber, polyphenols (including phenolic acids, flavonoids, and condensed tannins), policosanols, unsaturated fatty acids, and the food attribute of a high antioxidant capacity. However, the vast majority of studies utilized extracts or purified compounds and were conducted in animal models. Few studies in humans have been reported, and there is a need to study sorghum as a whole grain, and in the context of a healthy diet.

High-quality clinical research investigating effects of sorghum consumption in humans is the next step to build on the promising in vitro and animal research conducted to date. Human evidence for the long-term effects of consuming sorghum as part of a healthy diet is necessary to provide future directions for consumers, the food industry, growers, health professionals, and government-based grain advocacy organizations. If proven effective, the quality evidence from trials involving humans could position sorghum as an important driver for economic development in many of the world's most food-insecure regions, particularly parts of Africa, where sorghum is often the only viable grain food. This same evidence from human studies could also act as a catalyst for the uptake and demand for sorghum by food industry and consumers where the food supply is more plentiful and obesity is a problem.

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